

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference  P318A	<b>FOR FURTHER ACTION</b> <small>see Form PCT/ISA/220 as well as, where applicable, item 5 below.</small>	
International application No.  PCT/EP2005/050899	International filing date (day/month/year)  01/03/2005	(Earliest) Priority Date (day/month/year)  02/03/2004
Applicant  EPFL ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 8 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (See Box II).

3. ☐ **Unity of invention is lacking** (see Box III).

**4. With regard to the title,**

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

**5. With regard to the abstract,**

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

**6. With regard to the drawings,**

a. the figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☒ none of the figures is to be published with the abstract.

# INTERNATIONAL SEARCH REPORT

International application No.

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## Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
  - a. type of material
    - ☒ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material
    - ☒ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing
    - ☒ contained in the international application as filed
    - ☐ filed together with the international application in computer readable form
    - ☐ furnished subsequently to this Authority for the purpose of search
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

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## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N9/10 C12N15/62 G01N33/535

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>GENDREIZIG S ET AL: "Induced protein dimerization in vivo through covalent labeling"</p> <p>JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, DC, US,</p> <p>vol. 125, no. 49,</p> <p>12 August 2003 (2003-08-12), pages 14970-14971, XP002293223</p> <p>ISSN: 0002-7863</p> <p>page 14970, left-hand column, paragraph 3 - right-hand column, paragraph 1</p> <p>-----</p> <p>-/--</p>	9-37



Further documents are listed in the continuation of box C:



Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is, taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

13 October 2005

Date of mailing of the international search report

24/10/2005

Name and mailing address of the ISA

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Authorized officer

Barnas, C

## INTERNATIONAL SEARCH REPORT

 International Application No  
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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	JUILLERAT A ET AL: "Directed evolution of 06-alkylguanine-DNA alkyltransferase for efficient labeling of fusion proteins with small molecules in vivo" CHEMISTRY AND BIOLOGY, CURRENT BIOLOGY, LONDON, GB, vol. 10, no. 4, April 2003 (2003-04), pages 313-317, XP002288298 ISSN: 1074-5521 table 1	9-37
Y	STEMMER W P C: "RAPID EVOLUTION OF A PROTEIN IN VITRO BY DNA SHUFFLING" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 370, 4 August 1994 (1994-08-04), pages 389-391, XP002082182 ISSN: 0028-0836 page 389, right-hand column, paragraph 2 - page 390, right-hand column, paragraph 4	9-37
Y	WO 98/13487 A (MAXYGEN, INC) 2 April 1998 (1998-04-02) claims 1-11 figures 1-3	9-37
Y	XU-WELLIVER M ET AL: "Point mutations at multiple sites including highly conserved amino acids maintain activity, but render 06-alkylguanine-DNA alkyltransferase insensitive to 06-benzylguanine" BIOCHEMICAL JOURNAL, THE BIOCHEMICAL SOCIETY, LONDON, GB, vol. 347, no. 2, 15 April 2000 (2000-04-15), pages 519-526, XP002273210 ISSN: 0264-6021 tables 3,4,6 page 523, right-hand column, paragraphs 2,3	9-37
A	WO 02/083937 A (ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE; JOHNSON, KAI; GENDREIZIG, S) 24 October 2002 (2002-10-24) page 3, paragraph 1 page 7, lines 14-17	9-37
P, X	WO 2004/031404 A (ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE ; JUILLERAT, ALEXANDRE; KEPPL) 15 April 2004 (2004-04-15) claims 20-31	9-37
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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>WO 2004/031405 A (ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE ; KINDERMANN, MAIK; JOHNSSON,) 15 April 2004 (2004-04-15) example 58</p> <p>-----</p>	9-37

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 1-8

Present claims 1-7 relate to a compound which has a given desired property or effect, namely an O6-alkylguanine-DNA alkyltransferase (ATG) mutant with specific properties as listed in claims 1-7 when compared to the wild type human ATG. Claim 8 defines its subject matter by a process (product by process claim) and is therefore directed to a product (ATG) as such. The sequence of ATG is, however, an inherent feature thereof that does not contain any information if it has been modified or not. Similarly, an ATG does not contain any information if one of its characteristics has been improved by a genetic modification or not. As a consequence, claims 1-7 cover all ATGs having the properties described therein and claim 8 covers all ATGs with the properties of claims 1-7 and a sequence embraces by the broad definition of said claim.

However, the description does not provide support and disclosure in the sense of Article 6 and 5 PCT for any such compound having the said property or effect and there is no common general knowledge of this kind available to the person skilled in the art. This non-compliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search of the claim (PCT Guidelines 9.19 and 9.20).

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

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## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1-8  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No  
PCT/EP2005/050899

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9813487	A	02-04-1998	AU 4503797 A CA 2266423 A1 EP 0964922 A1 JP 2001504325 T	17-04-1998 02-04-1998 22-12-1999 03-04-2001
WO 02083937	A	24-10-2002	CA 2443570 A1 CN 1527941 A EP 1410023 A2 JP 2004532028 T NZ 528594 A NZ 537939 A ZA 200307442 A	24-10-2002 08-09-2004 21-04-2004 21-10-2004 29-07-2005 26-08-2005 21-04-2004
WO 2004031404	A	15-04-2004	AU 2003267423 A1 CA 2501061 A1	23-04-2004 15-04-2004
WO 2004031405	A	15-04-2004	AU 2003271669 A1 CA 2501063 A1	23-04-2004 15-04-2004